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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,842	05/02/2007	Jo Klaveness	PN0396	7406

36335 7590 08/26/2010

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EXAMINER	
SAMALA, JAGADISHWAR RAO	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
08/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,842	KLAVENESS ET AL.	
	Examiner	Art Unit	
	JAGADISHWAR R. SAMALA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Group I, claims 1-9 and 12 in the reply filed on 08/19/2010 is acknowledged.

- Claims 1-9 and 12 are pending in the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 06/14/2006 was noted and the submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 and 12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an optical imaging contrast agent with an affinity for an abnormally expressed biological target associated with prostate cancer of formula (I),

V-L-R, wherein V is one or more vector moieties having affinity for an abnormally expressed target in prostate cancer, L is a linker moiety or a bond and R is one or more reporter moieties detectable in in-vivo optical imaging, and wherein the contrast agent has a molecular weight below 14000 Daltons. However, the claims are devoid of any structural elements that correlate to the function which is to be achieved with the claimed composition. For example, a vast numbers of potential "vector moieties have an affinity for an abnormally expressed target in prostate cancer may be found in the art to be capable of having the claimed function. The specification discloses examples of some variety of targets for which the vector may have affinity including steroid 5 alpha-reductase, COX-2, prostate specific antigen … (page 7 and 8). Such targets are widely varying in structure and would have an almost unlimited number of potential vectors which may have affinity thereto. It is clear that Applicant had possession of such a few specific formulations at the time of filing using specific and defined vectors as identified in page 7 and 8 and the Examples, but the specification as originally filed does not provide support that Applicant had possession of the invention as generically claimed by function alone in the instant claims. Applicant's limited disclosure of a particular compound which has the claimed functional properties does not provide support that Applicant envisaged the invention as a whole which is broadly claimed solely by function. In the instant case, a definition by function alone does not appear to sufficiently describe the claimed invention because it is only an indication of what the agent does, rather than what it is. See MPEP 2163 and Eli Lilly, 119 F.3 at 1568, 43 USPQ2d at 1406.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Weissleder et al (US 2003/0044353)

Claims are drawn to an optical imaging contrast agent with affinity for an abnormally expressed biological target associated with prostate cancer.

Weissleder teaches activatable imaging probes that include a chromophore attachment moiety and one or more chromophores, such as near-infrared chromophores, chemically linked to the chromophore attachment moiety so that upon activation of the imaging probe the optical properties of the plurality of chromophores are altered. The probe optionally includes protective chains or chromophore spacers, or both. Also disclosed are methods of using the imaging probes for optical imaging (abstract). A number of specific peptide substrates including cathepsin D-specific peptide substrates, MMP, PSA substrates, thrombin substrates and others are included in the probes of the present invention (e.g., 0075, Table 2). Cathepsin D is also disclosed as a target. Spacers containing the amino acid sequence recognized by cathepsin D can be used to produce an imaging probe that undergoes activation specifically in breast cancer tissue. An example of a cathepsin D-sensitive spacer is the

oligopeptide: Gly-Pro-Ile-Cys-Phe-Phe-Arg-Leu-Gly (SEQ ID NO:l). Other cathepsin D-sensitive spacers can be designed using information known in the art regarding the substrate specificity of cathepsin D. See, e.g., Gulnik et al, 1977, FEBS Let, 413, 379-384 (0070). Exemplary chromophores include cyanine (cy5.5, cy5, cy7) (0062, Table 1 and Examples). Pharmaceutical compositions include sterile injectable solutions including isotonic saline, etc. (paragraph 0128-0129). See also Examples.

Regarding the limitation of the instant claims wherein the optical contrast agent has an "affinity for an abnormally expressed biological target associated with prostate cancer," it is noted that cathepsin D is associated with prostate cancer, as evidenced by Applicant's specification at page 6. The intended use of the vector as "having affinity for an abnormally expressed target in affinity for an abnormally expressed biological target associated with prostate cancer " has not been given patentable weight to distinguish over Weissleder because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, and then it meets the claim. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Since Weissleder discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claims 1-9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Lauffer et al (US 2002/0034476).

Claims are drawn to an optical imaging contrast agent with affinity for an abnormally expressed biological target associated with prostate cancer.

Lauffer teaches diagnostic MRI and optical imaging prodrug contrast agents for the sensitive detection of a specific bioactivity within a tissue, and pharmaceutically acceptable derivatives thereof (0013). The prodrug contrast agent comprises an image-enhancing moiety (IEM); a protein binding moiety (PMB); and a modification site (MS) (0036 and claim 1). Also disclosed are methods of using these compositions and compounds for MRI and optical imaging (0014). A specific modification site useful for diagnostic agents for prostate cancer includes is one which is altered by prostate-specific antigen (PSA), a serine protease glycoprotein produced exclusively by prostatic tissue. PSA is extremely useful for monitoring therapy, particularly prostatectomy because its presence is decreased to nearly zero following removal of the prostate (0100 and Table III). The pharmaceutical compositions may be in the form of sterile injectable preparations, for e.g., sterile injectable aqueous or oleaginous suspensions including Ringer's solution and isotonic sodium chloride solution (0124).

Regarding the limitation of the instant claims wherein the optical contrast agent has an "affinity for an abnormally expressed biological target associated with prostate cancer," it is noted that Prostate-specific antigen is associated with prostate cancer, as evidenced by Applicant's specification at page 8. The intended use of the vector as "having affinity for an abnormally expressed target in affinity for an abnormally expressed biological target associated with prostate cancer " has not been given patentable weight to distinguish over Lauffer because the intended use of the claimed

invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, and then it meets the claim. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Since Lauffer discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-9 and12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Klaveness et al (US 6,264,914) in view of Lauffer et al (US 2002/0034476).

Claims are drawn to an optical imaging contrast agent with affinity for an abnormally expressed biological target associated with prostate cancer.

Klaveness discloses compositions of the formula V-L-R, where V is a vector moiety having affinity for an angiogenesis-related endothelial cell receptor, L is a linker moiety or a bond and R is a detectable moiety (abstract). Characterized in the composition, V is a non-peptidic compound having affinity for AII receptors, linker component is a bond between the vector and reporter moieties include organic chromophoric or fluorophoric dyes (col. 27 lines 45+). The compositions may be formulated using physiologically acceptable carrier suitable for patenteral or enteral administration. Additional disclosure includes that formula V-L-R may be therapeutically effective in the treatment of disease states as well as detectable in in vivo imaging. Thus for example the vector on the reporter moieties may have therapeutic efficacy, eg. by virtue of the radiotherapeutic effect of a radionuclide reporter, the efficacy in photodynamic therapy of a chromophore (fluorophore) reporter or the chemotherapeutic effect of the vector moiety.

Klaveness fails to teach imaging prostate cancer via prostate-specific antigen targeting.

Lauffer teaches diagnostic MRI and optical imaging prodrug contrast agents for the sensitive detection of a specific bioactivity within a tissue, and pharmaceutically acceptable derivatives thereof (0013). The prodrug contrast agent comprises an image-enhancing moiety (IEM); a protein binding moiety (PMB); and a modification site (MS) (0036 and claim 1). Also disclosed are methods of using these compositions and compounds for MRI and optical imaging (0014). A specific modification site useful for diagnostic agents for prostate cancer includes is one which is altered by prostate-

specific antigen (PSA), a serine protease glycoprotein produced exclusively by prostatic tissue. PSA is extremely useful for monitoring therapy, particularly prostatectomy because its presence is decreased to nearly zero following removal of the prostate (0100 and Table III).

Regarding the limitation of the instant claims wherein the optical contrast agent has an "affinity for an abnormally expressed biological target associated with prostate cancer," it is noted that Prostate-specific antigen is associated with prostate cancer, as evidenced by Applicant's specification at page 8. The intended use of the vector as "having affinity for an abnormally expressed target in affinity for an abnormally expressed biological target associated with prostate cancer " has not been given patentable weight to distinguish over Lauffer because the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, and then it meets the claim. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Since Lauffer discloses compounds that are the same as those claimed, they would be capable of performing the intended use, as claimed.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate prostate-specific antigen targeting moiety into Klaveness composition. The person of ordinary skill in the art would have been motivated to make those modifications because Lauffer teaches that prostate-specific antigen (PSA) is extremely useful for monitoring therapy, particularly prostatectomy

because its presence is decreased to nearly zero following removal of the prostate. A slow rise in PSA following prostatectomy indicates that either not the entire prostate is removed or that lymph node metastases are present and producing the antigen. Therefore, person of ordinary skill in the art would have had a reasonable expectation of success because both Klaveness and Lauffer teaches compositions comprising diagnostic agents that can be used in the same filed of endeavor such as for magnetic resonance imaging and optical imaging and effective in the treatment of disease states as well as detectable in in-vivo imaging.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422

F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-9 and12 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/573,604, 10/573,606, 10/582,680 and 10/582,893. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to an optical imaging contrast agent with an affinity for an abnormally expressed biological target associated with prostate cancer having formula V-L-R, wherein V is one or more vector moieties having affinity for abnormally expressed target in prostate cancer. The claims of the '604, '606, '680, and '893 applications are drawn to optical contrast agents having formula V-L-R, wherein V has an affinity for abnormally expressed targets associated with endometriosis, colorectal cancer, atherosclerotic plaque, and lung cancer, respectively. The specifications of the instant application and those of the '604, '606, '680, and '893

applications, the vectors having affinity for various abnormally expressed biological targets may be the same (e.g. vectors for angiogenesis targets, adhesion molecules, estrogen receptors, metalloproteinases, e-cadherin, cathepsin B, etc.). The contrast agents are the same and should be capable of the same functions. Accordingly the claims are overlapping in scope and are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAGADISHWAR R. SAMALA whose telephone number is (571)272-9927. The examiner can normally be reached on 8.30 A.M to 5.00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571)272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. R. S./
Examiner, Art Unit 1618

/Jake M. Vu/
Primary Examiner, Art Unit 1618